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Comparative Effectiveness of Screening Strategies for Colorectal Cancer

Afsaneh Barzi, MD, PhD,
Assistant Professor of Medicine, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA

Heinz-Josef Lenz, MD,
Professor of Clinical Medicine, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA

David I. Quinn, MD, PhD,
Associate Professor of Medicine, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA

Sarmad Sadeghi, MD, PhD
Assistant Professor of Medicine, Norris Comprehensive Cancer Center, University of Southern California, 1441 Eastlake Ave, Suite 3440, Los Angeles, CA 90033

Abstract

Background—Screening for colorectal cancer (CRC) has been successful in decreasing the incidence and mortality from CRC. While new screening tests have become available, their relative impact on CRC outcomes remains unexplored. This study compares the outcomes of various screening strategies on CRC outcomes.

Methods—A Markov model representing the natural history of CRC was built and validated against empiric data from screening trials as well as the Microstimulation Screening Analysis (MISCAN) model. Thirteen screening strategies based on colonoscopy, sigmoidoscopy, computed tomographic colonography, as well as fecal immunochemical, occult blood, and stool DNA testing were compared with no screening. A simulated sample of the US general population ages 50 to 75 years with an average risk of CRC was followed for up to 35 years or until death. Effectiveness

Corresponding Author: Sarmad Sadeghi, MD, PhD, Assistant Professor of Medicine, Norris Comprehensive Cancer Center, University of Southern California, 1441 Eastlake Ave, Suite 3440, Los Angeles, CA 90033, Phone: 323-865-0553, Fax: 323-865-0061, Sarmad.Sadeghi@usc.edu.

Afsaneh Barzi, MD, PhD
Contribution: Study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis; technical, or material support; study supervision

Sarmad Sadeghi, MD, PhD
Contribution: Study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis; technical, or material support; study supervision

Heinz-Josef Lenz, MD
Contribution: analysis and interpretation of data; critical revision of the manuscript for important intellectual content;

David I. Quinn, MD, PhD
Contribution: analysis and interpretation of data; critical revision of the manuscript for important intellectual content;

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was measured by discounted life years gained and the number of CRCs prevented. Discounted costs and cost-effectiveness ratios were calculated. A discount rate of 3% was used in calculations. The study took a societal perspective.

Results—Colonoscopy emerged as the most effective screening strategy with the highest life years gained (0.022 life years) and CRCs prevented (n = 1068) and the lowest total costs ($2861). These values were 0.012 life years gained, 574 CRCs prevented, and a total cost of $3164, respectively, for FOBT; and 0.011 life years gained, 647 CRCs prevented, and a total cost of $4296, respectively, for DNA testing. Improved sensitivity or specificity of a screening test for CRC detection was not sufficient to close the outcomes gap compared with colonoscopy.

Conclusions—Improvement in CRC detection performance is not sufficient to improve screening outcomes. Special attention must be directed to detecting precancerous adenomas.

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States, with an estimated incidence of 134,490 new cases and 49,190 deaths in 2016. This represents a decline in incidence and mortality that is primarily attributable to increased screening and removal of precancerous adenomas, and a smaller but measureable contribution from risk factor modification and improved treatments[1–3]. Screening for CRC can reduce its incidence of colorectal cancer[4–7], might result in a stage shift favoring earlier stage at diagnosis[8, 9], and has the theoretical benefit of reducing the costs of care.

With rising costs of care for CRC as a result of newer and more expensive drugs and the improved overall survival as a result of these treatments, screening for CRC becomes even more important as the alternative becomes increasingly more expensive. A detailed study of the interactions between downstream societal outcomes of screening and the multitude of strategies available for screening is only possible through modeling.

To explore these dynamics, we evaluated various CRC screening strategies and compared them along different sets of measures of effectiveness, costs, and cost effectiveness. We examined how improved sensitivity and specificity of a screening test for detection of CRC impacts its effectiveness. We also investigated how one could *engineer* and define a hypothetical screening test that would be competitive to the best among these strategies by exploring the performance characteristics of this hypothetical test for detection of adenomas.

Methods

We used modeling and individual-level simulation (microsimulation) to measure and compare the benefits of screening for CRC in the US population. The study took a societal perspective, and costs and effects were discounted at the standard rate of 3%. The model, assumptions, and analyses conformed to best practices[10,11] and to recommendations of the US Panel on Cost-Effectiveness in Health and Medicine[12] and the Agency for Healthcare Research and Quality.[13] Screening test characteristics are summarized in Table 1,[14–27] and a complete list of assumptions and corresponding references is available in the Supplementary Materials (see online supporting information).

Study Design

Thirteen screening strategies (ST 1 through ST 13) were compared with no screening as the referent strategy. Each screening *strategy* comprised 1 or 2 screening *tests* that would be performed over prescribed intervals. The following screening strategies were evaluated:

1) ST 1: Fecal occult blood testing (FOBT) annually
2) ST 2: Fecal immunochemical testing (FIT) annually
3) ST 3: FOBT annually and flexible sigmoidoscopy (Flex Sig) every 5 years
4) ST 4: FIT annually and Flex Sig every 5 years
5) ST 5: Colonoscopy every 10 years (3 or 5 years, with adenoma)
6) ST 6: Flex Sig every 5 years
7) ST 7: FOBT 2 (FOBT every other year)
8) ST 8: FIT 2 (FIT every other year)
9) ST 9: FOBT 2 and Flex Sig every 5 years
10) ST 10: FIT 2 + Flex Sig every 5 years
11) ST 11: DNA (stool DNA testing annually)
12) ST 12: DNA 2 (stool DNA testing every other year)
13) ST 13: Computed tomography (CT) colonography every 10 years

Events, including screening tests, cancer diagnoses, treatment, and mortality, and the associated costs were recorded. The effectiveness of each screening strategy was measured in life years (LY) and reductions in cancer incidence and mortality. Costs of screening tests were based on Centers for Medicare and Medicaid payments and published material in peer-reviewed articles. A second cost estimate for screening tests that included patient out-of-pocket expenses was also used.[28,29] These cost models were designated cost models A and B, respectively, and simulations were run using both models.

Costs of cancer therapy were inclusive of the newer therapeutic agents used as part of standard of care. A Cost Effectiveness Analysis (CEA) was performed and Incremental Cost Effectiveness Ratios (ICERs) for each strategy calculated.

Study Population

The study population was designed to be representative of the US general population in terms of age, sex, and risk for CRC using data from Surveillance, Epidemiology, and End Results (SEER) program.[30,31] The incidence of CRC in the non-screened population was modeled using SEER incidence data from 1990 and 1995 (before the presumed impact of screening incidence reduction was reflected in the SEER data) and the incidence reduction attributable to screening was modeled using long-term lower endoscopy data[6, 31]. Individuals diagnosed with colorectal cancer were staged in a manner representative of stage distribution for screened and non-screened populations[8, 9, 31] as appropriate and treatments were offered in keeping with standards of care[32]. Individual preferences for compliance with screening was modeled using published data for various screening modalities. Mortality, colorectal cancer specific and non-specific, were modeled based on stage specific mortality for colorectal cancer[8], and US life tables[33].

One hundred thousand individual members of the US population with average risk for colorectal cancer aged 50 to 75, as described above, were simulated and followed for up to 35 years or until the time of death.

CRC Model

A Markov model was built to represent the CRC incidence and its natural history in individual members of the US general population. The performance parameters of the screening tests (ie, sensitivity and specificity), were assumed to be conditionally independent of repeat screening.[29] All positive screening tests for all strategies (except colonoscopy) resulted in a "diagnostic" colonoscopy. In the event of a negative diagnostic colonoscopy, 2 distinct possibilities were modeled for future screening:

a. Upgrading the screening strategy to colonoscopy in a manner consistent with colonoscopy based screening strategy (Base Case)

b. Resuming the original screening strategy after a period recommended by diagnostic colonoscopy (Alternate Case)

In both cases, simulated individuals were subjected to the CRC risk reduction associated with colonoscopy.[31] Stage shift, in the form of a lower probability of distant metastases at the time of diagnosis for the screened population, was modeled using data from the literature.[8]

The impact of adenomas was modeled by attributing the observed incidence reduction associated with colonoscopy, and sigmoidoscopy to the removal of precancerous adenomas.

All simulations were performed using TreeAge Pro 2015 by TreeAge Software, Inc.

Outcome Measures

Primary and secondary outcome measures were defined as described below.

Effectiveness and Comparative Effectiveness—The primary effectiveness outcome measure for each strategy was defined in terms of discounted life years.

A secondary effectiveness outcome measure was defined as the total number of "prevented" CRCs during simulation as a result of screening.

Costs—Discounted total strategy costs, costs of screening, and costs of cancer care were calculated as cost outcome measures.

Cost Effectiveness—ICERs using discounted, incremental total strategy costs and incremental life years gained (LYG) were used as the cost-effectiveness outcome measure. A willingness to pay of $50,000 per LYG was used as a guide to identify the cost-effective strategies.[34,35] If a strategy was not cost-effective, then it was designated as dominated. Absolute dominance (AD) indicates that the next strategy is more effective and less costly, and extended dominance (ED) indicates that the next strategy is more effective and costlier but has a lower ICER.

Sensitivity and Exploratory Analyses

Several one-way sensitivity analyses were performed. DNA testing is associated with a modest adenoma detection sensitivity that was included in the analysis to examine the impact of adenoma detection on effectiveness of the screening strategy[19, 23]. The effect of increasing compliance with screening under both Base and Alternate cases was explored. A sensitivity analysis assuming similar stage distribution for screened and non-screened populations, rejecting the stage shift assumption, was performed.

To explore the maximal benefits achievable by DNA testing, the sensitivity and specificity of the DNA test were both set at 100%, and simulations were performed.

To define the characteristics of an ideal screening test, we performed a series of 2-way analyses to explore how a hypothetical strategy could approach or outperform the most effective strategy. “Test X” was defined with performance parameters similar to the most effective stool-testing screening strategy. By using colonoscopy as the benchmark, the sensitivity of “Test X” for the detection of precancerous polyps was defined relative to that of colonoscopy with a range from 50% to 100%. A proportionate benefit in terms of incidence reduction in CRCs for the simulated individuals was given to those screened with “Test X.” A sensitivity analysis was performed over this range to determine the point at which “Test X” would dominate the most effective screening strategy by being more effective or rendering it no longer cost effective. Three strategies based on “Test X” were included with screening intervals yearly, every 3 years and every 5 years.

Validation of the Model

The model was validated by comparison of its predictions with empiric data from clinical studies as well as the widely accepted model for CRC, Microstimulation Screening Analysis (MISCAN). Schoen et al[36] reported an incidence reduction of 26% (95% confidence interval [CI], 13%–37%) and a mortality reduction of 21% (95% CI, 15%–28%), given a compliance rate of 83%. In this model, when compliance was set at 80%, the percentage of cancer cases prevented (incidence reduction) increased to 27%, which was within the 95% confidence interval of Schoen et al, and the mortality risk was reduced by 38%, which was marginally higher than that reported by Schoen et al.

Given the inevitable difference between a representative sample of the population and the conditions of a clinical trial, there would be differences, but they would be small and could be explained by differences in age, comorbidities, follow-up duration, baseline risk, compliance, and improved cancer survival over the years.

Under near perfect conditions, including enrolling individuals at age 50 years and screening them with a 100% compliance until age 75, MISCAN predicted 230 LYG per 1000 screened individuals, an incidence risk reduction of 51.9% and a mortality reduction of 64.6% for colonoscopy.[16,28] These numbers, as predicted by the model, were 137 LYG per 1000 screened individuals, 39% and 46%, respectively. MISCAN investigators in discussing their results pointed out that their model might overestimate the benefits of screening based on the set up of their assumptions.[29] A more recent published study reporting simulation results

using MISCAN, shows a smaller benefit size for colonoscopy of 151.6 LYG per 1000 screened individuals aged 65 years.[7]

For further details, please see Supplementary Materials (see online supporting information).

Results

Unless otherwise specified, the results refer to the Base Case using cost model A.

Effectiveness

Colonoscopy emerged as the most effective strategy under the base and alternate cases. CT colonography and flexible sigmoidoscopy were the next 2 most effective strategies, respectively. DNA testing was more effective than FOBT and FIT by a small margin. The difference in effectiveness among strategies was modest with a maximum of 0.022 discounted LYG (1.2 weeks) for colonoscopy versus no screening. Screening was associated with a 5% to 23% relative-risk reduction and a 12% to 34% cancer-specific mortality risk reduction compared with no screening. The highest risk-reduction levels were associated with the colonoscopy strategy. The incidence of CRC was lowest for the colonoscopy strategy, despite performing a colonoscopy for all positive screening tests in the remaining strategies and accruing the resulting incidence reduction after a negative colonoscopy. Including the role of adenoma detection in DNA testing strategies improved their effectiveness by increasing LYG and the number of prevented cancers (Table 2). The results for the alternate case under cost model A are presented in Table 3.

Costs

Many screening strategies had costs that were significantly lower than the costs of treatment for CRC if no screening was offered. By using cost model A or B, DNA testing strategies were significantly more expensive than colonoscopy and no screening.

Cost Effectiveness

Colonoscopy dominated all strategies by being the most effective strategy at the lowest cost. The improvement in effectiveness and reduction in costs as a result of adding adenoma detection role for DNA testing at the reported 42.4% sensitivity failed to improve their cost effectiveness to a competitive level by remaining more costly and less effective than colonoscopy- Figure 1.

The costs of cancer management for DNA testing alone exceeded the total strategy costs for colonoscopy. Unless the cost of DNA testing was reduced to $29 or less per test and adenoma detection is included in its performance, DNA testing remained more expensive, and less effective than colonoscopy.

Tables 2 and 3, which include adenoma detection and enhancing the performance of DNA testing by setting its sensitivity and specificity for detection of cancer at 100%, failed to make DNA stool testing competitive with colonoscopy.

Sensitivity Analyses

With increasing compliance the effectiveness for all strategies increased and total strategy costs decreased. Colonoscopy remained the most effective strategy and had the lowest total strategy costs, dominating other strategies.

The baseline analysis included a 7% absolute risk reduction for a diagnosis of metastatic CRC in individuals undergoing screening. Eliminating this benefit for screening resulted in negligible changes in the effectiveness of strategies under the base and alternate case assumptions and cost models A and B. Colonoscopy continued to dominate other strategies in effectiveness, costs, and cost effectiveness, including DNA testing annually or every other year, when the adenoma-detection sensitivity was included in the analysis.

Exploratory Analysis and Hypothetical Test X

Under the base and alternate assumptions, using cost models A and B, the sensitivity for detecting adenoma of 3 strategies based on “Test X” performed at intervals of 1, 3, and 5 years was set at 50%, 60%, 70%, 80%, 90%, and 100%; and costs for “Test X” were varied between $25 and $500 per test at 7 cost points. The results indicated that, except at an adenoma-detection sensitivity of 100% for “Test X,” despite consistent improvement in its effectiveness, costs remained a problem, preventing it from dominating colonoscopy. At a cost per test of $200 or less, “Test X” dominated colonoscopy in 16 of 24 simulations (66%), and an adenoma-detection sensitivity ≥70% changed this ratio to 16 of 21 simulations (76%) (Table 4).

Discussion

Colonoscopy remained the most effective screening strategy across a wide range of sensitivity analyses. The total costs for colonoscopy were consistently the lowest among all strategies, making colonoscopy the dominant strategy in terms of effectiveness, costs, and cost-effectiveness. Choosing a different strategy resulted in lower effectiveness and higher costs, making such an option undesirable, from clinical, societal or public health standpoints. However, it must also be stated that choosing an alternative to colonoscopy may be necessary in day-to-day practice and for individual patients.

DNA stool testing, in its newest iteration (Cologuard), remained too expensive; and, even at costs approaching zero, it could not dominate colonoscopy in a CEA. This has been a concern for DNA stool testing.[38]

Even with higher sensitivity and specificity for detecting CRC compared with colonoscopy, DNA testing was not as effective as colonoscopy. The reason was traceable to the number of cancers prevented as a result of the detection of precancerous polyps.

Including a sensitivity of 50% for the detection of adenomas in DNA testing parameters (slightly higher than the sensitivity published for Cologuard[19,23]) started to close this gap. DNA testing, even at high sensitivities for adenoma detection, could not surpass colonoscopy with significant margins in terms of effectiveness. This was expected, because the sensitivity of DNA testing is measured relative to that of colonoscopy as the benchmark.

Therefore, at higher ends of the cost range for DNA testing, colonoscopy was more cost effective, although it was minimally less effective.

Stage shift is an interesting part of this picture. Although it is considered a benefit of screening, the SEER data, at least on the surface, were not reflective of a tangible change over the years in the frequency of metastatic CRC, regardless of whether it could be attributed to screening. In baseline analysis, we did include a stage shift, consistent with the best information available; however, when this effect was removed, the resulting changes were negligible across a wide range of the sensitivity analyses.

Although CT colonography was dominated by colonoscopy, it would be the next most cost-effective strategy among the remaining screening strategies. Whereas further research is needed into the efficacy of CT colonography, the optimal interval for such screening and its ability to reduce CRC incidence and mortality is warranted, these results indicate that it is an effective screening tool. Indeed, the US Preventive Services Task Force included CT colonography in its most recent recommendations.[39]

The current results clearly illustrate the challenge investigators face in their efforts to create a more effective screening test. As a means to achieve that goal, improving the sensitivity and specificity for detecting invasive cancer is not supported by these results. Instead, improving performance for the detection of adenomas would result in better outcomes.

It is conceivable that colonoscopy will remain the most effective test for CRC screening and intervention. It is also conceivable that, for the time being, stool tests may not have the sensitivity or specificity of colonoscopy for detecting precancerous lesions. However, there is potential for stool testing to identify cancerous and precancerous lesions even before they can be detected by colonoscopy; therefore, it remains a very worthwhile area of research. With increasing sensitivity for precancerous adenoma detection, stool testing can potentially exceed the sensitivity of colonoscopy, given the estimates that it may miss 10% of polyps.[40]

The cost analysis in this study indicates that screening with colonoscopy (and with many other modalities) resulted in lower overall costs compared with no screening. Although this is in contrast to the findings of some prior CEAs,[38] it is a reflection of the rising costs of care. In prior models, the costs of care did not include modern treatment options, such as oxaliplatin and bevacizumab.[41,42]

It may appear paradoxical that FOBT outperformed FIT, although it is a less sensitive test. This is because both tests are supplemented with colonoscopy in case of a positive result. Because FOBT triggers more colonoscopies due to the higher false-positive rate (lower specificity), more individuals accrue the benefits of colonoscopy.

The sensitivity analysis results indicate that “Test X” at longer intervals, with 100% compliance and a power to detect adenoma equal to that of colonoscopy, outperformed “Test X” at shorter intervals across all measures. This intriguing finding was traced to a reduction in the number of colonoscopies in longer interval applications of “Test X” due to fewer false-positive results.

The magnitude of the screening benefit in terms of LYG, incidence, and cancer mortality reduction predicted by this model were smaller compared with that predicted by the MISCAN model.[16,28] When adjusted for the differences in assumptions, the predictions of the current model were in range with those of the MISCAN model.

This study offers insights into what can be achieved by various screening strategies under specific assumptions. In everyday clinical practice, other realities such as capacity and access in the healthcare system as well as individual preferences also impact the magnitude and realization of the expected benefits.

The current study is limited because it is a modeled representation of the prevailing understanding of screening for CRC in lieu of a direct, head-to-head comparison of the strategies listed here. The study is also limited by its data sources. The cost assumptions in the model are derived from the US healthcare system; therefore, costs and cost-effectiveness results and discussions are primarily applicable within that healthcare system. Care must be exercised when applying these results to healthcare systems in other countries.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Condensed Abstract

Colonoscopy remains the most effective screening tool for colorectal cancer. DNA testing while interesting is costlier and is not as effective with an effectiveness gap that cannot be closed by improving the sensitivity and specificity of DNA testing for colorectal cancer.

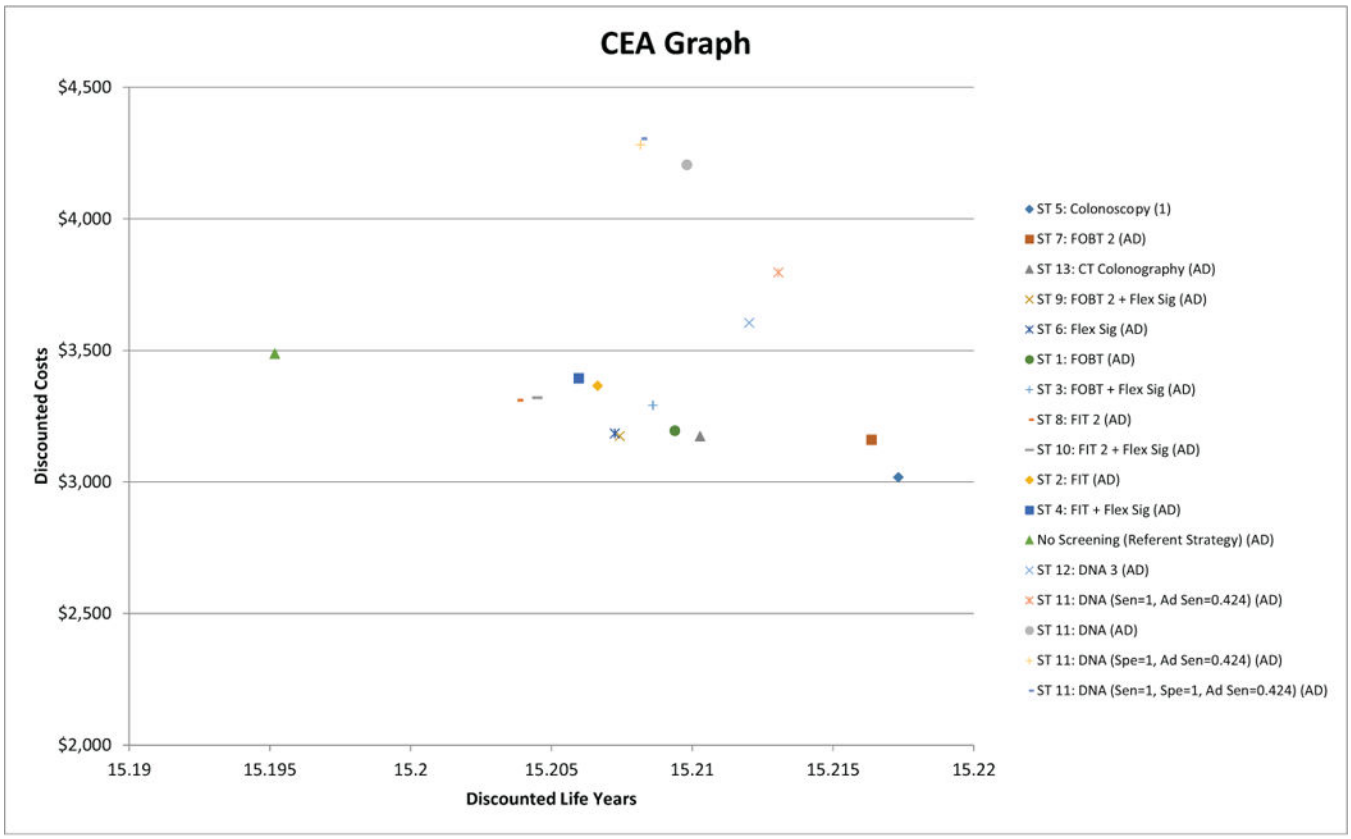

Figure 1.

Cost effectiveness graph.

Colonoscopy was the most effective strategy at the lowest cost (right lower corner of the graph) and dominated

all other strategies and was ranked number (1).

AD: Abdolute Dominance.

Ad Sen: Sensisitivity for detection of adenoma. Sen: Sensitivity for detection of invasive cancer. Spe: Specificity for detection of invasive cancer.

Table 1:

Screening test characteristics used in the analysis.

Test Characteristic	Value (Range)	Varied in Sensitivity Analysis	Source
Test Characteristic			
Sensitivity of FOBT	0.643 (0.356, 0.86)	No	14, 15
Sensitivity of FIT	0.818 (0.478, 0.968)	No	14, 15
Sensitivity of Colonoscopy	0.95 (0.92, 0.99)	No	15–17
Sensitivity of Diagnostic Colonoscopy	0.95 (0.92, 0.99)	No	15, 16
Sensitivity of Flex Sig	0.75 (0.72, 0.85)	No	15, 18
Sensitivity of DNA	0.923 (0.83, 0.975)	No	15, 19, 20
Sensitivity of CT Colonography	0.922 (0.84, .93)	No	15, 21, 22
Sensitivity of Test X (Set to match DNA)	0.923 (0.83, 0.975)	No	
Sensitivity of DNA Testing for Adenoma	0.424 (0.389–0.46)	No	15, 19, 20
Sensitivity of CT Colonography for Adenoma	0.8 (0.045–1)	No	15, 22
Sensitivity of Test X for Adenoma (relative to colonoscopy)	0.5 (0.5–1)	No	
Specificity of FOBT	0.901 (0.893, 0.908)	No	14, 15
Specificity of FIT	0.969 (0.964, 0.974)	No	14, 15
Specificity of Colonoscopy	0.9 (0.9, 1)	No	15, 16
Specificity of Diagnostic Colonoscopy	0.9 (0.9, 1)	No	15, 16
Specificity of Flex Sig	0.92 (0.92, 1)	No	15, 16, 18, 23
Specificity of DNA	0.866 (0.859, 0.872)	No	15, 19, 20
Specificity of CT Colonography	0.82 (0.796, 0.88)	No	15, 21, 22
Specificity of Test X (Set to match DNA)	0.866 (0.859, 0.872)	No	
Test Compliance			
Compliance Referent	1		
Compliance with FOBT	0.462 (0.462, 1)	Yes	24
Compliance with FIT- extrapolated using FOBT	0.462 (0.462, 1)	Yes	24
Compliance with FOBT + Flex Sig- extrapolated using Flex Sig	0.63 (0.63, 1)	Yes	25
Compliance with FIT + Flex Sig- extrapolated using Flex Sig	0.63 (0.63, 1)	Yes	25
Compliance with Colonoscopy- extrapolated using Flex Sig	0.63 (0.63, 1)	Yes	25, 26
Compliance with Flex Sig	0.63 (0.63, 1)	Yes	25
Compliance with FOBT 2	0.597 (0.597, 1)	Yes	24, 27
Compliance with FIT 2	0.597 (0.597, 1)	Yes	24, 27
Compliance with FOBT 2 + Flex Sig	0.63 (0.63, 1)	Yes	25
Compliance with FIT 2 + Flex Sig	0.63 (0.63, 1)	Yes	25
Compliance with DNA 1- extrapolated using FOBT	0.462 (0.462, 1)	Yes	24
Compliance with DNA 3- extrapolated using FOBT 2	0.597 (0.597, 1)	Yes	24, 27
Compliance with Test X - extrapolated using FOBT	0.462 (0.462, 1)	Yes	24
Compliance with Test X 3 - extrapolated using FOBT 2	0.597 (0.597, 1)	Yes	24, 27
Compliance with Test X 5- extrapolated using Flex Sig	0.63 (0.63, 1)	Yes	25

Test Characteristic	Value (Range)	Varied in Sensitivity Analysis	Source
Compliance with CT Colonography- extrapolated using Flex Sig	0.63 (0.63, 1)	Yes	25

Table 2

Results under Base Case and Cost Model A. Stage shift effect was included.

	Comparative Effectiveness						Costs			Cost Effectiveness			
Strategy	**Discounted LY**	**CRC Diagnosed**	**CRC Prevented**	**CRC Risk Reduction**	**CRC Deaths**	**Cancer Mortality Risk Reduction**	**Cancer Management**	**Screening**	**Total**	**Incremental Costs**	**Incremental Effect**	**ICER**	**Status (Rank)**
No Screening (Referent Strategy)	15.205	4,503	0	0%	1,310	0%	$ 3,415	$ –	$ 3,415	$ 554	−0.022	$ (−)	AD
ST 1: FOBT	15.215	3,944	574	12%	1,086	17%	$ 3,078	$ 86	$ 3,164	$ 303	−0.012	$ (−)	AD
ST 2: FIT	15.211	4,233	279	6%	1,156	12%	$ 3,180	$ 123	$ 3,303	$ 442	−0.016	$ (−)	AD
ST 3: FOBT + Flex Sig	15.217	3,863	655	14%	1,056	19%	$ 3,012	$ 158	$ 3,170	$ 309	−0.009	$ (−)	AD
ST 4: FIT + Flex Sig	15.214	4,135	380	8%	1,123	14%	$ 3,106	$ 232	$ 3,338	$ 477	−0.013	$ (−)	AD
ST 5: Colonoscopy	15.227	3,462	1,068	23%	863	34%	$ 2,335	$ 526	$ 2,861	$ –	0.000	$ 0	UD (1)
ST 6: Flex Sig	15.221	4,014	500	11%	1,029	21%	$ 2,875	$ 270	$ 3,145	$ 284	−0.006	$ (−)	AD
ST 7: FOBT 2	15.218	3,977	539	12%	1,052	20%	$ 2,979	$ 75	$ 3,054	$ 193	−0.009	$ (−)	AD
ST 8: FIT 2	15.215	4,284	222	5%	1,121	14%	$ 3,093	$ 93	$ 3,186	$ 325	−0.012	$ (−)	AD
ST 9: FOBT 2 + Flex Sig	15.219	3,915	603	13%	1,036	21%	$ 2,949	$ 178	$ 3,128	$ 267	−0.008	$ (−)	AD
ST 10: FIT 2 + Flex Sig	15.217	4,176	334	7%	1,090	17%	$ 3,026	$ 230	$ 3,256	$ 395	−0.010	$ (−)	AD
ST 11: DNA	15.216	3,870	647	14%	1,071	18%	$ 3,041	$ 1,255	$ 4,296	$ 1,435	−0.011	$ (−)	AD
ST 12: DNA 2	15.219	3,860	656	14%	1,031	21%	$ 2,929	$ 1,232	$ 4,161	$ 1,300	−0.008	$ (−)	AD
ST 13: CT Colonography [*]	15.225	3,594	930	20%	922	30%	$ 2,568	$ 494	$ 3,062	$ 201	−0.001	$ (−)	AD
ST 11: DNA (Sen=1, Ad Sen=0.424) [†]	15.218	3,762	758	16%	1,034	21%	$ 2,931	$ 1,255	$ 4,186	$ 1,325	−0.009	$ (−)	AD
ST 11: DNA (Spe=1, Ad Sen=0.424) [‡]	15.214	4,019	492	11%	1,099	16%	$ 2,936	$ 2,649	$ 5,585	$ 2,724	−0.012	$ (−)	AD
ST 11: DNA (Sen=1, Spe=1, Ad Sen=0.424) [§]	15.214	4,019	492	11%	1,099	16%	$ 2,936	$ 2,649	$ 5,585	$ 2,724	−0.012	$ (−)	AD

Comparisons of Effectiveness, Costs, and Cost Effectiveness measures.

LY: Life Years. CRC: Colorectal Cancer. ICER: Incremental Cost Effectiveness Ratio. (−) negative value. AD: Absolute Dominance. UD: Undominated. Ad Sen: Adenoma Sensitivity. Sen: CRC Sensitivity. Spe: CRC Specificity.

[*] CT colonography had a reported sensitivity of 80% for detection of adenomas. Therefore, a proportional CRC risk reduction was given to this strategy.

[†] A sensitivity of 100% for CRC and a sensitivity of 42.4% for detection of adenomas was given to DNA test. Results shown for comparison.

[‡] A specificity of 100% for CRC and a sensitivity of 42.4% for detection of adenomas was given to DNA test. Results shown for comparison.

[§] A sensitivity and a specificity of 100% for CRC and a sensitivity of 42.4% for detection of adenomas was given to DNA test. Results shown for comparison.

Table 3

Results under Base Case and Cost Model B. Stage shift effect was excluded.

	Comparative Effectiveness						Costs			Cost Effectiveness			
Strategy	**Discounted LY**	**CRC Diagnosed**	**CRC Prevented**	**CRC Risk Reduction**	**CRC Deaths**	**Cancer Mortality Risk Reduction**	**Cancer Management**	**Screening**	**Total**	**Incremental Costs**	**Incremental Effect**	**ICER**	**Status (Rank)**
No Screening (Referent Strategy)	15.199	4,483	0	0%	1,380	0%	$ 3,494	$ –	$ 3,494	$ 463	−0.022	$ (−)	AD
ST 1: FOBT	15.209	4,093	398	9%	1,167	15%	$ 3,258	$ 16	$ 3,274	$ 243	−0.012	$ (−)	AD
ST 2: FIT	15.205	4,327	161	3%	1,238	10%	$ 3,338	$ 100	$ 3,438	$ 407	−0.015	$ (−)	AD
ST 3: FOBT + Flex Sig	15.210	4,017	476	10%	1,138	18%	$ 3,217	$ 85	$ 3,303	$ 272	−0.011	$ (−)	AD
ST 4: FIT + Flex Sig	15.207	4,231	258	6%	1,188	14%	$ 3,256	$ 207	$ 3,463	$ 432	−0.013	$ (−)	AD
ST 5: Colonoscopy	15.221	3,453	1,052	23%	954	31%	$ 2,504	$ 526	$ 3,030	$ –	0.000	$ 0	UD (1)
ST 6: Flex Sig	15.210	4,055	439	10%	1,172	15%	$ 3,104	$ 256	$ 3,360	$ 330	−0.011	$ (−)	AD
ST 7: FOBT 2	15.210	4,132	356	8%	1,160	16%	$ 3,234	$ 14	$ 3,247	$ 217	−0.011	$ (−)	AD
ST 8: FIT 2	15.206	4,354	131	3%	1,228	11%	$ 3,294	$ 74	$ 3,368	$ 337	−0.015	$ (−)	AD
ST 9: FOBT 2 + Flex Sig	15.210	4,098	395	9%	1,148	17%	$ 3,213	$ 119	$ 3,332	$ 301	−0.010	$ (−)	AD
ST 10: FIT 2 + Flex Sig	15.208	4,256	231	5%	1,175	15%	$ 3,233	$ 206	$ 3,440	$ 409	−0.012	$ (−)	AD
ST 11: DNA	15.210	4,033	460	10%	1,156	16%	$ 3,255	$ 1,469	$ 4,724	$ 1,694	−0.011	$ (−)	AD
ST 12: DNA 2	15.210	4,062	426	9%	1,143	17%	$ 3,222	$ 1,333	$ 4,555	$ 1,524	−0.011	$ (−)	AD
ST 13: CT Colonography [*]	15.217	3,622	880	19%	1,026	26%	$ 2,766	$ 491	$ 3,258	$ 227	−0.004	$ (−)	AD
ST 11: DNA (Sen=1, Ad Sen=0.424) [†]	15.212	3,832	664	15%	1,096	21%	$ 3,082	$ 1,469	$ 4,551	$ 1,521	−0.009	$ (−)	AD
ST 11: DNA (Spe=1, Ad Sen=0.424) [‡]	15.209	4,004	489	11%	1,148	17%	$ 3,032	$ 2,654	$ 5,686	$ 2,656	−0.012	$ (−)	AD
ST 11: DNA (Sen=1, Spe=1, Ad Sen=0.424) [§]	15.209	4,004	489	11%	1,148	17%	$ 3,032	$ 2,654	$ 5,686	$ 2,656	−0.012	$ (−)	AD

Comparisons of Effectiveness, Costs, and Cost Effectiveness measures.

LY: Life Years. CRC: Colorectal Cancer. ICER: Incremental Cost Effectiveness Ratio. (−) negative value. AD: Absolute Dominance. UD: Undominated. Ad Sen: Adenoma Sensitivity. Sen: CRC Sensitivity. Spe: CRC Specificity.

[*] CT colonography had a reported sensitivity of 80% for detection of adenomas. Therefore, a proportional CRC risk reduction was given to this strategy.

[†] A sensitivity of 100% for CRC and a sensitivity of 42.4% for detection of adenomas was given to DNA test. Results shown for comparison.

[‡] A specificity of 100% for CRC and a sensitivity of 42.4% for detection of adenomas was given to DNA test. Results shown for comparison.

[§] A sensitivity and a specificity of 100% for CRC and a sensitivity of 42.4% for detection of adenomas was given to DNA test. Results shown for comparison.

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Table 4

Exploratory two-way analysis for the adenoma detection sensitivity and cost for Test X. Comparisons made only for colonoscopy strategy as the domiannt strategy in the primary analyses and 3 strategies built on Test X.

			Comparative Effectiveness			Cost Effectiveness																													
						Test × Costs = $25				Test × Costs = $75				Test × Costs = $150				Test × Costs = $200				Test × Costs = $300				Test × Costs = $400				Test × Costs = $500			
Assumptions	Sensitivity for Adenoma Detection	Strategy	LY	CRC Diagnosed	CRC Prevented	Costs	ICER	Status (Rank)		Costs	ICER	Status (Rank)		Costs	ICER	Status (Rank)		Costs	ICER	Status (Rank)		Costs	ICER	Status (Rank)		Costs	ICER	Status (Rank)		Costs	ICER	Status (Rank)	
Base Case Cost Model A	50 %	ST 5: Colonoscopy	15.215	3,521	1,032	$ 3,001	$ 46,231	UD (2)		$ 3,001	$ 11,296	UD (2)		$ 3,001	$ 0	UD (1)		$ 3,001	$ 0	UD (1)		$ 3,001	$ 0	UD (1)		$ 3,001	$ 0	UD (1)		$ 3,001	$ 0	UD (1)	
		ST 14: Test X	15.231	3,787	760	$ 3,037	$ (–)	AD		$ 3,154	$ (–)	AD		$ 3,329	$ (–)	AD		$ 3,445	$ (–)	AD		$ 3,679	$ (–)	AD		$ 3,912	$ (–)	AD		$ 4,150	$ (–)	AD	
		ST 15: Test X 3	15.232	3,643	903	$ 2,880	$ 0	UD (1)		$ 2,973	$ 12,668	ED		$ 3,113	$ (–)	AD		$ 3,207	$ (–)	AD		$ 3,393	$ (–)	AD		$ 3,579	$ (–)	AD		$ 3,770	$ (–)	AD	
		ST 16: Test X 5	15.231	3,757	790	$ 2,888	$ (–)	AD		$ 2,957	$ 0	UD (1)		$ 3,062	$ (–)	AD		$ 3,132	$ (–)	AD		$ 3,272	$ (–)	AD		$ 3,411	$ (–)	AD		$ 3,554	$ (–)	AD	
	60 %	ST 5: Colonoscopy	15.218	3,492	1,068	$ 3,149	$ 100,657	UD (2)		$ 3,149	$ 71,782	UD (2)		$ 3,149	$ 20,469	UD (2)		$ 3,149	$ 0	UD (1)		$ 3,149	$ 0	UD (1)		$ 3,149	$ 0	UD (1)		$ 3,149	$ 0	UD (1)	
		ST 14: Test X	15.211	3,747	807	$ 3,174	$ (–)	AD		$ 3,291	$ (–)	AD		$ 3,465	$ (–)	AD		$ 3,582	$ (–)	AD		$ 3,815	$ (–)	AD		$ 4,049	$ (–)	AD		$ 4,287	$ (–)	AD	
		ST 15: Test X 3	15.215	3,555	1,003	$ 2,917	$ (–)	AD		$ 3,011	$ (–)	AD		$ 3,150	$ (–)	AD		$ 3,244	$ (–)	AD		$ 3,430	$ (–)	AD		$ 3,617	$ (–)	AD		$ 3,807	$ (–)	AD	
		ST 16: Test X 5	15.215	3,647	910	$ 2,905	$ 0	UD (1)		$ 2,975	$ 0	UD (1)		$ 3,080	$ 0	UD (1)		$ 3,150	$ (–)	AD		$ 3,290	$ (–)	AD		$ 3,430	$ (–)	AD		$ 3,572	$ (–)	AD	
	70 %	ST 5: Colonoscopy	15.218	3,470	1,024	$ 2,910	$ 105,984	UD (2)		$ 2,910	$ 73,999	UD (2)		$ 2,910	$ 26,021	UD (2)		$ 2,910	$ 0	UD (1)		$ 2,910	$ 0	UD (1)		$ 2,910	$ 0	UD (1)		$ 2,910	$ 0	UD (1)	
		ST 14: Test X	15.211	3,680	801	$ 2,970	$ (–)	AD		$ 3,086	$ (–)	AD		$ 3,260	$ (–)	AD		$ 3,376	$ (–)	AD		$ 3,608	$ (–)	AD		$ 3,840	$ (–)	AD		$ 4,072	$ (–)	AD	
		ST 15: Test X 3	15.216	3,461	1,024	$ 2,703	$ (–)	AD		$ 2,796	$ (–)	AD		$ 2,936	$ (–)	AD		$ 3,029	$ (–)	AD		$ 3,215	$ (–)	AD		$ 3,401	$ (–)	AD		$ 3,587	$ (–)	AD	
		ST 16: Test X 5	15.216	3,547	942	$ 2,679	$ 0	UD (1)		$ 2,749	$ 0	UD (1)		$ 2,853	$ 0	UD (1)		$ 2,923	$ (–)	AD		$ 3,063	$ (–)	AD		$ 3,202	$ (–)	AD		$ 3,342	$ (–)	AD	
	80 %	ST 5: Colonoscopy	15.199	3,576	1,027	$ 3,073	$ 477,084	UD (3)		$ 3,073	$ 353,451	UD (2)		$ 3,073	$ 202,133	UD (2)		$ 3,073	$ 101,254	UD (2)		$ 3,073	$ 0	UD (1)		$ 3,073	$ 0	UD (1)		$ 3,073	$ 0	UD (1)	
		ST 14: Test X	15.192	3,803	788	$ 3,162	$ (–)	AD		$ 3,279	$ (–)	AD		$ 3,454	$ (–)	AD		$ 3,571	$ (–)	AD		$ 3,804	$ (–)	AD		$ 4,037	$ (–)	AD		$ 4,270	$ (–)	AD	
		ST 15: Test X 3	15.199	3,506	1,093	$ 2,786	$ 302,875	UD (2)		$ 2,880	$ 564,770	ED		$ 3,020	$ 957,615	ED		$ 3,114	$ (–)	AD		$ 3,300	$ (–)	AD		$ 3,487	$ (–)	AD		$ 3,674	$ (–)	AD	
		ST 16: Test X 5	15.198	3,578	1,023	$ 2,759	$ 0	UD (1)		$ 2,829	$ 0	UD (1)		$ 2,934	$ 0	UD (1)		$ 3,003	$ 0	UD (1)		$ 3,143	$ (–)	AD		$ 3,282	$ (–)	AD		$ 3,422	$ (–)	AD	
	90 %	ST 5: Colonoscopy	15.225	3,591	1,007	$ 3,057	$ (–)	AD		$ 3,057	$ (–)	AD		$ 3,057	$ (–)	AD		$ 3,057	$ (–)	AD		$ 3,057	$ (–)	AD		$ 3,057	$ 0	UD (1)		$ 3,057	$ 0	UD (1)	
		ST 14: Test X	15.222	3,742	852	$ 2,940	$ (–)	AD		$ 3,056	$ (–)	AD		$ 3,230	$ (–)	AD		$ 3,346	$ (–)	AD		$ 3,578	$ (–)	AD		$ 3,810	$ (–)	AD		$ 4,042	$ (–)	AD	
		ST 15: Test X 3	15.225	3,427	1,149	$ 2,659	$ (–)	AD		$ 2,752	$ (–)	AD		$ 2,892	$ (–)	AD		$ 2,986	$ (–)	AD		$ 3,172	$ (–)	AD		$ 3,359	$ (–)	AD		$ 3,545	$ (–)	AD	
		ST 16: Test X 5	15.225	3,490	1,110	$ 2,628	$ 0	UD (1)		$ 2,698	$ 0	UD (1)		$ 2,802	$ 0	UD (1)		$ 2,872	$ 0	UD (1)		$ 3,012	$ 0	UD (1)		$ 3,152	$ 303,965	UD (2)		$ 3,291	$ 751,893	UD (2)	
	100%	ST 5: Colonoscopy	15.198	3,536	1,030	$ 3,032	$ (–)	AD		$ 3,032	$ (–)	AD		$ 3,032	$ (–)	AD		$ 3,032	$ (–)	AD		$ 3,032	$ (–)	AD		$ 3,032	$ (–)	AD		$ 3,032	$ 0	UD (1)	
		ST 14: Test X	15.193	3,681	890	$ 3,004	$ (–)	AD		$ 3,120	$ (–)	AD		$ 3,295	$ (–)	AD		$ 3,412	$ (–)	AD		$ 3,645	$ (–)	AD		$ 3,878	$ (–)	AD		$ 4,112	$ (–)	AD	
		ST 15: Test X 3	15.201	3,278	1,293	$ 2,571	$ (–)	AD		$ 2,665	$ (–)	AD		$ 2,804	$ (–)	AD		$ 2,897	$ (–)	AD		$ 3,084	$ (–)	AD		$ 3,270	$ (–)	AD		$ 3,456	$ (–)	AD	
		ST 16: Test X 5	15.201	3,333	1,238	$ 2,503	$ 0	UD (1)		$ 2,572	$ 0	UD (1)		$ 2,677	$ 0	UD (1)		$ 2,747	$ 0	UD (1)		$ 2,886	$ 0	UD (1)		$ 3,026	$ 0	UD (1)		$ 3,165	$ 36,504	UD (2)	
Alternate Case Cost Model A	50 %	ST 5: Colonoscopy	15.199	3,503	909	$ 3,021	$ 94,226	UD (2)		$ 3,021	$ 48,963	UD (2)		$ 3,021	$ 0	UD (1)		$ 3,021	$ 0	UD (1)		$ 3,021	$ 0	UD (1)		$ 3,021	$ 0	UD (1)		$ 3,021	$ 0	UD (1)	
		ST 14: Test X	15.191	3,835	644	$ 3,103	$ (–)	AD		$ 3,249	$ (–)	AD		$ 3,468	$ (–)	AD		$ 3,614	$ (–)	AD		$ 3,905	$ (–)	AD		$ 4,197	$ (–)	AD		$ 4,490	$ (–)	AD	
		ST 15: Test X 3	15.196	3,674	805	$ 2,805	$ 0	UD (1)		$ 2,909	$ 0	UD (1)		$ 3,064	$ (–)	AD		$ 3,168	$ (–)	AD		$ 3,376	$ (–)	AD		$ 3,584	$ (–)	AD		$ 3,796	$ (–)	AD	
		ST 16: Test X 5	15.194	3,773	706	$ 2,861	$ (–)	AD		$ 2,936	$ (–)	AD		$ 3,048	$ (–)	AD		$ 3,123	$ (–)	AD		$ 3,273	$ (–)	AD		$ 3,423	$ (–)	AD		$ 3,576	$ (–)	AD	
	60 %	ST 5: Colonoscopy	15.209	3,529	1,041	$ 3,016	$ 41,032	UD (2)		$ 3,016	$ 18,181	UD (2)		$ 3,016	$ 0	UD (1)		$ 3,016	$ 0	UD (1)		$ 3,016	$ 0	UD (1)		$ 3,016	$ 0	UD (1)		$ 3,016	$ 0	UD (1)	
		ST 14: Test X	15.200	3,837	729	$ 3,158	$ (–)	AD		$ 3,303	$ (–)	AD		$ 3,521	$ (–)	AD		$ 3,666	$ (–)	AD		$ 3,957	$ (–)	AD		$ 4,248	$ (–)	AD		$ 4,544	$ (–)	AD	
		ST 15: Test X 3	15.205	3,640	923	$ 2,862	$ 0	UD (1)		$ 2,966	$ 47,627	ED		$ 3,122	$ (–)	AD		$ 3,226	$ (–)	AD		$ 3,434	$ (–)	AD		$ 3,642	$ (–)	AD		$ 3,854	$ (–)	AD	
		ST 16: Test X 5	15.204	3,744	826	$ 2,864	$ (–)	AD		$ 2,939	$ 0	UD (1)		$ 3,051	$ (–)	AD		$ 3,126	$ (–)	AD		$ 3,276	$ (–)	AD		$ 3,426	$ (–)	AD		$ 3,579	$ (–)	AD	
	70 %	ST 5: Colonoscopy	15.211	3,543	1,020	$ 2,978	$ 62,598	UD (3)		$ 2,978	$ 43,216	UD (2)		$ 2,978	$ 14,768	UD (2)		$ 2,978	$ 0	UD (1)		$ 2,978	$ 0	UD (1)		$ 2,978	$ 0	UD (1)		$ 2,978	$ 0	UD (1)	
		ST 14: Test X	15.205	3,758	800	$ 2,954	$ (–)	AD		$ 3,069	$ (–)	AD		$ 3,318	$ (–)	AD		$ 3,463	$ (–)	AD		$ 3,754	$ (–)	AD		$ 4,046	$ (–)	AD		$ 4,343	$ (–)	AD	
		ST 15: Test X 3	15.207	3,558	1,003	$ 2,742	$ 54,077	UD (2)		$ 2,846	$ 203,631	ED		$ 3,002	$ (–)	AD		$ 3,107	$ (–)	AD		$ 3,315	$ (–)	AD		$ 3,523	$ (–)	AD		$ 3,736	$ (–)	AD	
		ST 16: Test X 5	15.207	3,641	922	$ 2,732	$ 0	UD (1)		$ 2,807	$ 0	UD (1)		$ 2,920	$ 0	UD (1)		$ 2,995	$ (–)	AD		$ 3,145	$ (–)	AD		$ 3,295	$ (–)	AD		$ 3,449	$ (–)	AD	
	80 %	ST 5: Colonoscopy	15.200	3,491	1,046	$ 2,972	$ 132,699	UD (2)		$ 2,972	$ 96,378	UD (2)		$ 2,972	$ 52,126	UD (2)		$ 2,972	$ 22,624	UD (2)		$ 2,972	$ 0	UD (1)		$ 2,972	$ 0	UD (1)		$ 2,972	$ 0	UD (1)	
		ST 14: Test X	15.193	3,678	858	$ 2,976	$ (–)	AD		$ 3,121	$ (–)	AD		$ 3,340	$ (–)	AD		$ 3,485	$ (–)	AD		$ 3,777	$ (–)	AD		$ 4,068	$ (–)	AD		$ 4,365	$ (–)	AD	

			Comparative Effectiveness			Cost Effectiveness																				
						Test × Costs = $25			Test × Costs = $75			Test × Costs = $150			Test × Costs = $200			Test × Costs = $300			Test × Costs = $400			Test × Costs = $500		
Assumptions	Sensitivity for Adenoma Detection	Strategy	LY	CRC Diagnosed	CRC Prevented	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)
		ST 15: Test X 3	15.197	3,402	1,136	**$ 2,641**	**$ 0**	**UD (1)**	$ 2,745	$ 354,029	ED	$ 2,901	$ 1,185,813	ED	$ 3,005	$ (−)	AD	$ 3,213	$ (−)	AD	$ 3,421	$ (−)	AD	$ 3,634	$ (−)	AD
		ST 16: Test X 5	15.197	3,486	1,057	$ 2,651	$ (−)	AD	**$ 2,726**	**$ 0**	**UD (1)**	**$ 2,839**	**$ 0**	**UD (1)**	$ 2,914	$ 0	UD (1)	$ 3,065	$ (−)	AD	$ 3,215	$ (−)	AD	$ 3,368	$ (−)	AD
	90%	ST 5: Colonoscopy	15.202	3,490	1,053	$ 3,025	$ (−)	AD	$ 3,025	$ (−)	AD	$ 3,025	$ (−)	AD	$ 3,025	$ (−)	AD	$ 3,025	$ (−)	AD	**$ 3,025**	**$ 0**	**UD (1)**	**$ 3,025**	**$ 0**	**UD (1)**
		ST 14: Test X	15.195	3,626	916	$ 2,982	$ (−)	AD	$ 3,129	$ (−)	AD	$ 3,349	$ (−)	AD	$ 3,495	$ (−)	AD	$ 3,788	$ (−)	AD	$ 4,081	$ (−)	AD	$ 4,380	$ (−)	AD
		ST 15: Test X 3	15.203	3,302	1,242	**$ 2,557**	**$ 9,385**	**UD (2)**	**$ 2,661**	**$ 36,935**	**UD (2)**	$ 2,817	$ 78,261	UD (2)	$ 2,922	$ 105,812	UD (2)	$ 3,130	$ 160,914	UD (2)	$ 3,339	$ 294,357	UD (2)	$ 3,551	$ 493,876	UD (2)
		ST 16: Test X 5	15.202	3,381	1,163	$ 2,547	$ 0	UD (1)	$ 2,622	$ 0	UD (1)	**$ 2,735**	**$ 0**	**UD (1)**	**$ 2,810**	**$ 0**	**UD (1)**	**$ 2,961**	**$ 0**	**UD (1)**	$ 3,111	$ 7,487,781	ED	$ 3,264	$ 20,846,524	ED
	100%	ST 5: Colonoscopy	15.207	3,477	1,060	$ 3,053	$ (−)	AD	$ 3,053	$ (−)	AD	$ 3,053	$ (−)	AD	$ 3,053	$ (−)	AD	$ 3,053	$ (−)	AD	$ 3,053	$ (−)	AD	$ 3,053	$ 0	UD (1)
		ST 14: Test X	15.206	3,527	1,005	$ 2,877	$ (−)	AD	$ 3,023	$ (−)	AD	$ 3,242	$ (−)	AD	$ 3,387	$ (−)	AD	$ 3,679	$ (−)	AD	$ 3,971	$ (−)	AD	$ 4,268	$ (−)	AD
		ST 15: Test X 3	15.210	3,149	1,393	$ 2,498	$ (−)	AD	$ 2,602	$ (−)	AD	$ 2,758	$ (−)	AD	$ 2,862	$ (−)	AD	$ 3,070	$ (−)	AD	$ 3,278	$ (−)	AD	$ 3,490	$ (−)	AD
		ST 16: Test X 5	15.212	3,235	1,309	**$ 2,422**	**$ 0**	**UD (1)**	**$ 2,497**	**$ 0**	**UD (1)**	**$ 2,609**	**$ 0**	**UD (1)**	**$ 2,684**	**$ 0**	**UD (1)**	**$ 2,834**	**$ 0**	**UD (1)**	**$ 2,983**	**$ 0**	**UD (1)**	**$ 3,136**	**$ 17,602**	**UD (2)**
Base Case Cost Model B	50%	ST 5: Colonoscopy	15.186	3,492	1,028	$ 3,923	$ 80,809	UD (3)	$ 3,923	$ 62,370	UD (2)	**$ 3,923**	**$ 38,977**	**UD (2)**	**$ 3,923**	**$ 23,382**	**UD (2)**	**$ 3,923**	**$ 0**	**UD (1)**	**$ 3,923**	**$ 0**	**UD (1)**	**$ 3,923**	**$ 0**	**UD (1)**
		ST 14: Test X	15.178	3,784	726	$ 3,986	$ (−)	AD	$ 4,103	$ (−)	AD	$ 4,277	$ (−)	AD	$ 4,394	$ (−)	AD	$ 4,627	$ (−)	AD	$ 4,860	$ (−)	AD	$ 5,098	$ (−)	AD
		ST 15: Test X 3	15.183	3,620	888	$ 3,640	$ 67,867	UD (2)	$ 3,734	$ 91,940	ED	$ 3,874	$ 128,050	ED	$ 3,968	$ (−)	ED	$ 4,155	$ (−)	AD	$ 4,342	$ (−)	AD	$ 4,533	$ (−)	AD
		ST 16: Test X 5	15.182	3,736	771	**$ 3,573**	**$ 0**	**UD (1)**	**$ 3,643**	**$ 0**	**UD (1)**	$ 3,748	$ 0	UD (1)	$ 3,818	$ 0	UD (1)	$ 3,958	$ (−)	AD	$ 4,097	$ (−)	AD	$ 4,240	$ (−)	AD
	60%	ST 5: Colonoscopy	15.216	3,498	1,023	$ 3,883	$ 86,563	UD (2)	$ 3,883	$ 69,381	UD (2)	**$ 3,883**	**$ 43,609**	**UD (2)**	**$ 3,883**	**$ 26,427**	**UD (2)**	**$ 3,883**	**$ 0**	**UD (1)**	**$ 3,883**	**$ 0**	**UD (1)**	**$ 3,883**	**$ 0**	**UD (1)**
		ST 14: Test X	15.210	3,717	799	$ 3,827	$ (−)	AD	$ 3,944	$ (−)	AD	$ 4,120	$ (−)	AD	$ 4,237	$ (−)	AD	$ 4,471	$ (−)	AD	$ 4,705	$ (−)	AD	$ 4,944	$ (−)	AD
		ST 15: Test X 3	15.211	3,552	967	$ 3,552	$ (−)	AD	$ 3,645	$ (−)	AD	$ 3,785	$ (−)	AD	$ 3,878	$ (−)	AD	$ 4,064	$ (−)	AD	$ 4,251	$ (−)	AD	$ 4,441	$ (−)	AD
		ST 16: Test X 5	15.212	3,654	868	**$ 3,531**	**$ 0**	**UD (1)**	**$ 3,601**	**$ 0**	**UD (1)**	$ 3,706	$ 0	UD (1)	$ 3,776	$ 0	UD (1)	$ 3,916	$ (−)	AD	$ 4,056	$ (−)	AD	$ 4,198	$ (−)	AD
	70%	ST 5: Colonoscopy	15.200	3,598	994	$ 3,950	$ 235,646	UD (3)	$ 3,950	$ 181,858	UD (3)	$ 3,950	$ 120,075	UD (2)	$ 3,950	$ 91,763	UD (2)	**$ 3,950**	**$ 35,138**	**UD (2)**	**$ 3,950**	**$ 0**	**UD (1)**	**$ 3,950**	**$ 0**	**UD (1)**
		ST 14: Test X	15.194	3,801	782	$ 3,845	$ (−)	AD	$ 3,961	$ (−)	AD	$ 4,136	$ (−)	AD	$ 4,253	$ (−)	AD	$ 4,487	$ (−)	AD	$ 4,720	$ (−)	AD	$ 4,958	$ (−)	AD
		ST 15: Test X 3	15.198	3,595	994	$ 3,542	$ 85,569	UD (2)	$ 3,635	$ 117,141	UD (2)	$ 3,774	$ 164,499	ED	$ 3,868	$ 196,071	ED	$ 4,054	$ (−)	AD	$ 4,240	$ (−)	AD	$ 4,430	$ (−)	AD
		ST 16: Test X 5	15.197	3,673	917	**$ 3,479**	**$ 0**	**UD (1)**	**$ 3,549**	**$ 0**	**UD (1)**	**$ 3,653**	**$ 0**	**UD (1)**	**$ 3,723**	**$ 0**	**UD (1)**	$ 3,863	$ 0	UD (1)	$ 4,003	$ (−)	AD	$ 4,145	$ (−)	AD
	80%	ST 5: Colonoscopy	15.208	3,514	1,052	$ 4,005	$ 1,946,310	UD (2)	$ 4,005	$ 1,717,452	UD (2)	$ 4,005	$ 1,374,166	UD (2)	$ 4,005	$ 1,145,309	UD (2)	$ 4,005	$ 687,595	UD (2)	$ 4,005	$ 229,881	UD (2)	**$ 4,005**	**$ 0**	**UD (1)**
		ST 14: Test X	15.200	3,736	817	$ 3,996	$ (−)	AD	$ 4,112	$ (−)	AD	$ 4,286	$ (−)	AD	$ 4,402	$ (−)	AD	$ 4,633	$ (−)	AD	$ 4,865	$ (−)	AD	$ 5,102	$ (−)	AD
		ST 15: Test X 3	15.206	3,430	1,135	$ 3,532	$ (−)	AD	$ 3,625	$ (−)	AD	$ 3,764	$ (−)	AD	$ 3,857	$ (−)	AD	$ 4,043	$ (−)	AD	$ 4,230	$ (−)	AD	$ 4,419	$ (−)	AD
		ST 16: Test X 5	15.207	3,472	1,093	**$ 3,412**	**$ 0**	**UD (1)**	**$ 3,482**	**$ 0**	**UD (1)**	**$ 3,586**	**$ 0**	**UD (1)**	**$ 3,656**	**$ 0**	**UD (1)**	**$ 3,795**	**$ 0**	**UD (1)**	**$ 3,935**	**$ 0**	**UD (1)**	$ 4,077	$ (−)	AD
	90%	ST 5: Colonoscopy	15.197	3,540	1,031	$ 4,039	$ (−)	AD	$ 4,039	$ (−)	AD	$ 4,039	$ (−)	AD	$ 4,039	$ (−)	AD	$ 4,039	$ (−)	AD	$ 4,039	$ (−)	AD	$ 4,039	$ (−)	AD
		ST 14: Test X	15.195	3,701	866	$ 3,818	$ (−)	AD	$ 3,935	$ (−)	AD	$ 4,110	$ (−)	AD	$ 4,227	$ (−)	AD	$ 4,461	$ (−)	AD	$ 4,694	$ (−)	AD	$ 4,933	$ (−)	AD
		ST 15: Test X 3	15.198	3,360	1,212	$ 3,407	$ (−)	AD	$ 3,500	$ (−)	AD	$ 3,641	$ (−)	AD	$ 3,734	$ (−)	AD	$ 3,921	$ (−)	AD	$ 4,108	$ (−)	AD	$ 4,299	$ (−)	AD
		ST 16: Test X 5	15.200	3,418	1,153	**$ 3,310**	**$ 0**	**UD (1)**	**$ 3,380**	**$ 0**	**UD (1)**	**$ 3,485**	**$ 0**	**UD (1)**	**$ 3,555**	**$ 0**	**UD (1)**	**$ 3,695**	**$ 0**	**UD (1)**	**$ 3,835**	**$ 0**	**UD (1)**	**$ 3,978**	**$ 0**	**UD (1)**
	100%	ST 5: Colonoscopy	15.206	3,542	1,038	$ 4,138	$ (−)	AD	$ 4,138	$ (−)	AD	$ 4,138	$ (−)	AD	$ 4,138	$ (−)	AD	$ 4,138	$ (−)	AD	$ 4,138	$ (−)	AD	$ 4,138	$ (−)	AD
		ST 14: Test X	15.201	3,643	932	$ 3,973	$ (−)	AD	$ 4,090	$ (−)	AD	$ 4,266	$ (−)	AD	$ 4,383	$ (−)	AD	$ 4,618	$ (−)	AD	$ 4,853	$ (−)	AD	$ 5,092	$ (−)	AD
		ST 15: Test X 3	15.207	3,278	1,308	$ 3,392	$ (−)	AD	$ 3,486	$ (−)	AD	$ 3,626	$ (−)	AD	$ 3,720	$ (−)	AD	$ 3,908	$ (−)	AD	$ 4,095	$ (−)	AD	$ 4,287	$ (−)	AD
		ST 16: Test X 5	15.209	3,346	1,239	**$ 3,337**	**$ 0**	**UD (1)**	**$ 3,407**	**$ 0**	**UD (1)**	**$ 3,512**	**$ 0**	**UD (1)**	**$ 3,582**	**$ 0**	**UD (1)**	**$ 3,722**	**$ 0**	**UD (1)**	**$ 3,862**	**$ 0**	**UD (1)**	**$ 4,005**	**$ 0**	**UD (1)**
Alternate Case Cost Model B	50%	ST 5: Colonoscopy	15.228	3,527	1,068	**$ 3,910**	**$ 48,143**	**UD (2)**	**$ 3,910**	**$ 34,571**	**UD (2)**	**$ 3,910**	**$ 14,212**	**UD (2)**	**$ 3,910**	**$ 639**	**UD (2)**	**$ 3,910**	**$ 0**	**UD (1)**	**$ 3,910**	**$ 0**	**UD (1)**	**$ 3,910**	**$ 0**	**UD (1)**
		ST 14: Test X	15.217	3,832	748	$ 4,037	$ (−)	AD	$ 4,184	$ (−)	AD	$ 4,404	$ (−)	AD	$ 4,551	$ (−)	AD	$ 4,844	$ (−)	AD	$ 5,138	$ (−)	AD	$ 5,437	$ (−)	AD
		ST 15: Test X 3	15.222	3,733	856	$ 3,695	$ (−)	AD	$ 3,799	$ (−)	AD	$ 3,956	$ (−)	AD	$ 4,061	$ (−)	AD	$ 4,270	$ (−)	AD	$ 4,479	$ (−)	AD	$ 4,692	$ (−)	AD
		ST 16: Test X 5	15.222	3,840	748	$ 3,643	$ 0	UD (1)	$ 3,719	$ 0	UD (1)	$ 3,832	$ 0	UD (1)	$ 3,907	$ 0	UD (1)	$ 4,057	$ (−)	AD	$ 4,208	$ (−)	AD	$ 4,362	$ (−)	AD
	60%	ST 5: Colonoscopy	15.219	3,477	1,050	$ 3,853	$ 68,354	UD (2)	**$ 3,853**	**$ 49,092**	**UD (3)**	**$ 3,853**	**$ 16,246**	**UD (2)**	**$ 3,853**	**$ 16,246**	**UD (2)**	**$ 3,853**	**$ 0**	**UD (1)**	**$ 3,853**	**$ 0**	**UD (1)**	**$ 3,853**	**$ 0**	**UD (1)**
		ST 14: Test X	15.211	3,755	762	$ 3,788	$ (−)	AD	$ 3,935	$ (−)	AD	$ 4,300	$ (−)	AD	$ 4,300	$ (−)	AD	$ 4,592	$ (−)	AD	$ 4,885	$ (−)	AD	$ 5,183	$ (−)	AD
		ST 15: Test X 3	15.214	3,608	914	**$ 3,484**	**$ 0**	**UD (1)**	$ 3,588	$ 33,220	UD (2)	$ 3,848	$ 155,167	ED	$ 3,848	$ 155,167	ED	$ 4,056	$ (−)	AD	$ 4,264	$ (−)	AD	$ 4,477	$ (−)	AD
		ST 16: Test X 5	15.213	3,689	835	$ 3,494	$ (−)	AD	$ 3,569	$ 0	UD (1)	$ 3,756	$ 0	UD (1)	$ 3,756	$ 0	UD (1)	$ 3,906	$ (−)	AD	$ 4,056	$ (−)	AD	$ 4,209	$ (−)	AD
	70%	ST 5: Colonoscopy	15.205	3,590	959	$ 4,005	$ 232,391	UD (3)	$ 4,005	$ 187,455	UD (2)	$ 4,005	$ 140,232	UD (2)	$ 4,005	$ 108,751	UD (2)	**$ 4,005**	**$ 45,788**	**UD (2)**	**$ 4,005**	**$ 0**	**UD (1)**	**$ 4,005**	**$ 0**	**UD (1)**
		ST 14: Test X	15.198	3,774	767	$ 3,858	$ (−)	AD	$ 4,005	$ (−)	AD	$ 4,225	$ (−)	AD	$ 4,372	$ (−)	AD	$ 4,667	$ (−)	AD	$ 4,961	$ (−)	AD	$ 5,261	$ (−)	AD

			Comparative Effectiveness			Cost Effectiveness																										
						Test × Costs = $25			Test × Costs = $75			Test × Costs = $150			Test × Costs = $200			Test × Costs = $300			Test × Costs = $400			Test × Costs = $500								
Assumptions	Sensitivity for Adenoma Detection	Strategy	LY	CRC Diagnosed	CRC Prevented	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)	Costs	ICER	Status (Rank)						
		ST 15: Test X 3	15.203	3,969	977	$ 3,572	$ 171,317	UD (2)	$ 3,677	$ 226,863	ED	$ 3,834	$ 316,182	ED	$ 3,938	$ 365,728	ED	$ 4,147	$ (-)	AD	$ 4,356	$ (-)	AD	$ 4,569	$ (-)	AD						
		ST 16: Test X 5	15.203	3,661	884	**$ 3,432**	**$ 0**	**UD (1)**	**$ 3,357**	**$ 0**	**UD (1)**	**$ 3,670**	**$ 0**	**UD (1)**	**$ 3,746**	**$ 0**	**UD (1)**	$ 3,896	$ 0	UD (1)	$ 4,047	$ (-)	AD	$ 4,200	$ (-)	AD						
		ST 5: Colonoscopy	15.236	3,573	1,025	$ 4,089	$ (-)	AD	$ 4,089	$ (-)	AD	$ 4,089	$ (-)	AD	$ 4,089	$ (-)	AD	$ 4,089	$ (-)	AD	$ 4,089	$ 93,335	UD (2)	**$ 4,089**	**$ 0**	**UD (1)**						
	80%	ST 14: Test X	15.231	3,733	858	$ 3,897	$ (-)	AD	$ 4,042	$ (-)	AD	$ 4,259	$ (-)	AD	$ 4,404	$ (-)	AD	$ 4,694	$ (-)	AD	$ 4,984	$ (-)	AD	$ 5,280	$ (-)	AD						
		ST 15: Test X 3	15.237	3,416	1,176	**$ 3,456**	**$ 0**	**UD (1)**	**$ 3,560**	**$ 27,255**	**UD (2)**	$ 3,716	$ 69,153	UD (2)	$ 3,820	$ 97,086	UD (2)	$ 4,028	$ 152,950	UD (2)	$ 4,236	$ 510,354	UD (3)	$ 4,448	$ 1,344,300	UD (2)						
		ST 16: Test X 5	15.236	3,551	1,045	$ 3,457	$ (-)	AD	$ 3,532	$ 0	UD (1)	**$ 3,644**	**$ 0**	**UD (1)**	**$ 3,719**	**$ 0**	**UD (1)**	**$ 3,869**	**$ 0**	**UD (1)**	**$ 4,019**	**$ 0**	**UD (1)**	$ 4,172	$ (-)	AD						
		ST 5: Colonoscopy	15.207	3,518	1,038	$ 3,949	$ (-)	AD	$ 3,949	$ (-)	AD	$ 3,949	$ (-)	AD	$ 3,949	$ (-)	AD	$ 3,949	$ (-)	AD	$ 3,949	$ (-)	AD	$ 3,949	$ (-)	AD						
	90%	ST 14: Test X	15.202	3,644	907	$ 3,790	$ (-)	AD	$ 3,937	$ (-)	AD	$ 4,158	$ (-)	AD	$ 4,305	$ (-)	AD	$ 4,599	$ (-)	AD	$ 4,893	$ (-)	AD	$ 5,193	$ (-)	AD						
		ST 15: Test X 3	15.208	3,326	1,231	$ 3,281	$ (-)	AD	$ 3,386	$ (-)	AD	$ 3,542	$ (-)	AD	$ 3,647	$ (-)	AD	$ 3,856	$ (-)	AD	$ 4,066	$ (-)	AD	$ 4,279	$ (-)	AD						
		ST 16: Test X 5	15.210	3,389	1,168	**$ 3,152**	**$ 0**	**UD (1)**	**$ 3,267**	**$ 0**	**UD (1)**	**$ 3,380**	**$ 0**	**UD (1)**	**$ 3,455**	**$ 0**	**UD (1)**	**$ 3,605**	**$ 0**	**UD (1)**	**$ 3,756**	**$ 0**	**UD (1)**	**$ 3,909**	**$ 0**	**UD (1)**						
		ST 5: Colonoscopy	15.203	3,510	1,096	$ 4,018	$ (-)	AD	$ 4,018	$ (-)	AD	$ 4,018	$ (-)	AD	$ 4,018	$ (-)	AD	$ 4,018	$ (-)	AD	$ 4,018	$ (-)	AD	$ 4,018	$ (-)	AD						
	100%	ST 14: Test X	15.197	3,627	997	$ 3,830	$ (-)	AD	$ 3,976	$ (-)	AD	$ 4,195	$ (-)	AD	$ 4,341	$ (-)	AD	$ 4,633	$ (-)	AD	$ 4,925	$ (-)	AD	$ 5,223	$ (-)	AD						
		ST 15: Test X 3	15.204	3,254	1,379	$ 3,304	$ (-)	AD	$ 3,408	$ (-)	AD	$ 3,564	$ (-)	AD	$ 3,668	$ (-)	AD	$ 3,876	$ (-)	AD	$ 4,084	$ (-)	AD	$ 4,296	$ (-)	AD						
		ST 16: Test X 5	15.205	3,328	1,307	**$ 3,218**	**$ 0**	**UD (1)**	**$ 3,294**	**$ 0**	**UD (1)**	**$ 3,406**	**$ 0**	**UD (1)**	**$ 3,482**	**$ 0**	**UD (1)**	**$ 3,632**	**$ 0**	**UD (1)**	**$ 3,782**	**$ 0**	**UD (1)**	**$ 3,931**	**$ 0**	**UD (1)**						

In each analysis, the most effective strategy with an ICER of less than a willingness to pay of $50,000 per life year gained was highlighted. If this strategy was colonoscopy it was highlighted in orange, if it was Test X, it was highlighted in green.

In each group of 6 rows an upper orange triangle and a lower green triangle were formed, indicating that Test X would be competitive to colnoscopy in the middle rows and columns

LY: Life Years. CRC: Colorectal Cancer. ICER: Incremental Cost Effectiveness Ratio. (−) negative value. AD: Absolute Dominance. ED: Extended Dominance. UD: Undominated.